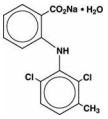
**MECLOFENAMATE SODIUM - meclofenamate sodium capsule**
Mylan Pharmaceuticals Inc.

**Rx only**

## DESCRIPTION

Meclofenamate sodium is N-(2,6-dichloro-m-tolyl) anthranilic acid, sodium salt, monohydrate. It is an anti-inflammatory drug for oral administration. Meclofenamate sodium capsules contain 50 mg or 100 mg meclofenamic acid as the sodium salt and the following inactive ingredients: colloidal silicon dioxide, FD&C Blue #1, gelatin, magnesium stearate, microcrystalline cellulose, pregelatinized starch, FD&C Red #3, sodium lauryl sulfate, titanium dioxide and D&C Yellow #10.
The structural formula of meclofenamate sodium is:




Molecular Formula: $C_{14}H_{10}Cl_2NNaO_2 \cdot H_2O$

It is a white to creamy white, odorless to almost odorless, crystalline powder with melting point 287° to 291°C, molecular weight 336.15, and it is freely soluble in water.

## CLINICAL PHARMACOLOGY

### Pharmacodynamics

Meclofenamate sodium is a non-steroidal agent which has demonstrated anti-inflammatory, analgesic, and antipyretic activity in laboratory animals. The mode of action, like that of other non-steroidal anti-inflammatory agents, is not known. Therapeutic action does not result from pituitary-adrenal stimulation. In animal studies, meclofenamate sodium was found to inhibit prostaglandin synthesis and to compete for binding at the prostaglandin receptor site. *In vitro*, meclofenamate sodium was found to be an inhibitor of human leukocyte 5-lipoxygenase activity. These properties may be responsible for the anti-inflammatory action of meclofenamate sodium. There is no evidence that meclofenamate sodium alters the course of the underlying disease.
In several human isotope studies, meclofenamate sodium, at a dosage of 300 mg/day, produced a fecal blood loss of 1 to 2 mL per day, and 2 to 3 mL per day at 400 mg/day. Aspirin, at a dosage of 3.6 g/day, caused a fecal blood loss of 6 mL per day.
In a multiple dose, one week study in normal human volunteers, meclofenamate sodium had little or no effect on collagen-induced platelet aggregation, platelet count, or bleeding time. In comparison, aspirin suppressed collagen-induced platelet aggregation and increased bleeding time. The concomitant administration of antacids (aluminum and magnesium hydroxides) does not interfere with absorption of meclofenamate sodium.

### Pharmacokinetics

Meclofenamate sodium is rapidly absorbed in man following single and multiple oral doses with peak plasma concentrations occurring in 0.5 to 2 hours. Based on a comparison to a suspension of meclofenamic acid, meclofenamate sodium is completely bioavailable.
The plasma concentrations of meclofenamic acid decline monoexponentially following oral administration. In a study in 10 healthy subjects following a single oral dose the apparent elimination half-life ranged from 0.8 to 5.3 hours. After the administration of meclofenamate sodium for 14 days every 8 hours, the apparent elimination half-life ranged from 0.8 to 2.1 hours with no evidence of accumulation of meclofenamic acid in plasma (see Table).
TABLE SUMMARY OF MECLOFENAMATE SODIUM PHARMACOKINETIC PARAMETERS

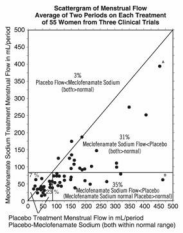
**Mean (Range) Parameter Values (n=10)**

| | **Meclofenamic Acid 100 mg*** | **Metabolite I†** |
|---|---|---|
| $C_{max}$ mcg/mL‡ | 4.8 (1.8 to 7.2) | 1.0 (0.5 to 1.5) |
| $t_{max}$ hr§ | 0.9 (0.5 to 1.5) | 2.4 (0.5 to 4.0) |
| $C_{min}$ mcg/mL¶ | 0.2 (0.5 to 1.5) | 0.4 (0.2 to 1.1) |
| Cl/F mL/min# | 206.0 (126 to 342) | --- |
| Vd/F liters Þ | 23.3 (9.1 to 43.2) | --- |
| $t_{1/2}$ hrß | 1.3 (0.8 to 2.1) | 15.3à |
| % of Dose in Urine Unconjugated | 0.0 --- | 0.5 (0 to 1.2) |
| Total | 2.7 (0 to 4.5) | 21.6 (7.5 to 32.6) |

*****Administered every 8 hours for 14 days
**†**3-Hydroxymethyl metabolite of meclofenamic acid with 20% activity of meclofenamate sodium *in vitro*
**‡**Peak plasma concentration
**§**Time to peak plasma concentration
**¶**Trough plasma concentration
**#**Oral clearance
**Þ**Oral distribution volume
**ß**Elimination half-life
**à**Estimated from mean data

Meclofenamic acid is extensively metabolized to an active metabolite (Metabolite I; 3-hydroxymethyl metabolite of meclofenamic acid) and at least six other less well characterized minor metabolites. Only this Metabolite I has been shown *in vitro* to inhibit cyclooxygenase activity with approximately one fifth the activity of meclofenamate sodium. Metabolite I (3-hydroxymethyl metabolite of meclofenamic acid) with a mean half-life of approximately 15 hours did accumulate following multiple dosing. After the administration of 100 mg meclofenamate sodium for 14 days every 8 hours, Metabolite I reached a peak plasma concentration of only 1 mcg/mL. By contrast, the peak concentration was 4.8 mcg/mL for the parent compound on both days 1 and 14. Therefore, the accumulation of Metabolite I is probably not clinically significant.
Approximately 70% of the administered dose is excreted by the kidneys with 8% to 35% excreted as predominantly conjugated species of meclofenamic acid and Metabolite I (see Table). Other metabolites, whose excretion rates are unknown, account for the remaining 35% to 62% of the dose excreted in the urine. The remainder of the administered dose (approximately 30%) is eliminated in the feces (apparently through biliary excretion). There is insufficient experience to know if meclofenamate sodium or its metabolites accumulate in patients with compromised renal or hepatic function. Therefore, meclofenamate sodium should be used with caution in these patients (see PRECAUTIONS). Trace amounts of meclofenamate sodium are excreted in human breast milk.
Meclofenamic acid is greater than 99% bound to plasma proteins over a wide drug concentration range.
Unlike most NSAIDs, which when administered with food have a decrease in rate but not in extent of absorption, meclofenamic acid is decreased in both. It has been reported that following the administration of meclofenamate sodium capsules one-half hour after a meal, the average extent of bioavailability decreased by 26%, the average peak concentration ($C_{max}$) decreased fourfold and the time to $C_{max}$ was delayed by 3 hours.

**Clinical Studies**
Controlled clinical trials comparing meclofenamate sodium with aspirin demonstrated comparable efficacy in rheumatoid arthritis. The meclofenamate sodium treated patients had fewer reactions involving the special senses, specifically tinnitus, but more gastrointestinal reactions, specifically diarrhea.
The incidence of patients who discontinued therapy due to adverse reactions was similar for both the meclofenamate sodium and aspirin-treated groups.
The improvement with meclofenamate sodium reported by patients and the reduction of the disease activity as evaluated by both physicians and patients with rheumatoid arthritis are associated with a significant reduction in number of tender joints, severity of tenderness, and duration of morning stiffness.
The improvement reported by patients and as evaluated by physicians in patients treated with meclofenamate sodium for osteoarthritis is associated with a significant reduction in night pain, pain on walking, degree of starting pain, and pain on passive motion. The function of knee joints also improved significantly.
Meclofenamate sodium has been used in combination with gold salts or corticosteroids in patients with rheumatoid arthritis. Studies have demonstrated that meclofenamate sodium contributes to the improvement of patients' conditions while maintained on gold salts or corticosteroids. Data are inadequate to demonstrate that meclofenamate sodium in combination with salicylates produces greater improvement than that achieved with meclofenamate sodium alone.
In controlled clinical trials of patients with mild to moderate pain, meclofenamate sodium 50 mg provided significant pain relief. In these studies of episiotomy and dental pain, meclofenamate sodium 100 mg demonstrated additional benefit in some patients. The onset of analgesic effect was generally within one hour and the duration of action was 4 to 6 hours.
In controlled clinical trials of patients with dysmenorrhea, meclofenamate sodium 100 mg t.i.d. provided significant reduction in the symptoms associated with dysmenorrhea.
In randomized double-blind crossover trials of meclofenamate sodium 100 mg t.i.d. versus placebo in women with heavy menstrual blood loss (MBL), meclofenamate sodium treatment was usually associated with a reduction in menstrual flow.
The graph below is a scatter plot of menstrual flow from the average of two menstrual periods on meclofenamate sodium treatments (vertical axis) versus two menstrual periods on placebo (horizontal axis) for 55 women. Of note, although the amount of reduction in MBL was variable, some degree of reduction occurred in 90% of women in this study.




The points on the graph represent the mean MBL for each subject when treated for two periods with placebo and two periods with meclofenamate sodium. To ease in interpretation, the following examples may be helpful. Point A represents a woman who had MBL of 459 mL while on placebo, and 405 mL on meclofenamate sodium. Point B represents a woman who had MBL of 472 mL while on placebo, and 64 mL when treated with meclofenamate sodium.
In association with this reduction in menstrual blood loss, the duration of menses was decreased by one day; tampon/pad usage was decreased by an average of two per day on the two days of heaviest flow; and symptoms of dysmenorrhea were significantly reduced.

## INDICATIONS AND USAGE

Meclofenamate sodium is indicated for the relief of mild to moderate pain.
Meclofenamate sodium is also indicated for the treatment of primary dysmenorrhea and for the treatment of idiopathic heavy menstrual blood loss (see CLINICAL PHARMACOLOGY and PRECAUTIONS).
Meclofenamate sodium is also indicated for relief of the signs and symptoms of acute and chronic rheumatoid arthritis and osteoarthritis. As with all non-steroidal anti-inflammatory drugs, selection of meclofenamate sodium requires a careful assessment of the benefit/risk ratio (see WARNINGS, PRECAUTIONS and ADVERSE REACTIONS).
Meclofenamate sodium is not recommended in children because adequate studies to demonstrate safety and efficacy have not been carried out.

## CONTRAINDICATIONS

Meclofenamate sodium should not be used in patients who have previously exhibited hypersensitivity to it.
Because the potential exists for cross-sensitivity to aspirin or other non-steroidal anti-inflammatory drugs, meclofenamate sodium should not be given to patients in whom these drugs induce symptoms of bronchospasm, allergic rhinitis, or urticaria.

## WARNINGS

### Risk of GI Ulceration, Bleeding and Perforation with NSAID Therapy

Serious gastrointestinal toxicity, such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated chronically with NSAID therapy. Although minor upper gastrointestinal problems, such as dyspepsia, are common, usually developing early in therapy, physicians should remain alert for ulceration and bleeding in patients treated chronically with NSAIDs even in the absence of previous GI tract symptoms. In patients observed in clinical trials of several months to two years duration, symptomatic upper GI ulcers, gross bleeding or perforation appear to occur in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for one year. Physicians should inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur.
Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Except for a prior history of serious GI events and other risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (e.g., age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well than other individuals, and most spontaneous reports of fatal GI events are in this population. Studies to date are inconclusive concerning the relative risk of various NSAIDs in causing such reactions. High doses of any NSAID probably carry a greater risk of these reactions, although controlled clinical trials showing this do not exist in most cases. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity.

## PRECAUTIONS

### General

Patients receiving non-steroidal anti-inflammatory agents, such as meclofenamate sodium, should be evaluated periodically to insure that the drug is still necessary and well tolerated (see other PRECAUTIONS, WARNINGS, and ADVERSE REACTIONS).
Diarrhea, gastrointestinal irritation and abdominal pain may be associated with meclofenamate sodium therapy. Dosage reduction or temporarily stopping the drug have generally controlled these symptoms (see ADVERSE REACTIONS andDOSAGE AND ADMINISTRATION).
Decreases in hemoglobin and/or hematocrit levels have occurred in approximately 1 of 6 patients, but rarely required discontinuation of meclofenamate sodium therapy. The clinical data revealed no evidence of increased chronic blood loss, bone marrow suppression, or hemolysis to account for the decreases in hemoglobin or hematocrit levels. Patients who are receiving long-term meclofenamate sodium therapy should have hemoglobin and hematocrit values determined if anemia is suspected on clinical grounds.

If a patient develops visual symptoms (see ADVERSE REACTIONS) during meclofenamate sodium therapy, the drug should be discontinued and the patient should have a complete ophthalmologic examination.
When meclofenamate sodium is used in combination with steroid therapy, any reduction in steroid dosage should be gradual to avoid the possible complications of sudden steroid withdrawal.

**Elderly**
Adverse effects are seen more commonly in the elderly; therefore, a lower starting dose and careful follow-up are advised.

**Evaluation of Patients with Heavy Menstrual Blood Loss**
Prior to prescribing meclofenamate sodium for heavy blood flow and primary dysmenorrhea, a thorough risk/benefit assessment should be made that takes into account the results described in the CLINICAL PHARMACOLOGY section. It is recommended that meclofenamate sodium treatment not be prescribed for heavy menstrual flow without establishing its idiopathic nature. Spotting or bleeding between cycles should be evaluated fully and not treated with meclofenamate sodium. Worsening of menstrual blood loss or excessive blood loss failing to respond to meclofenamate sodium should also be evaluated by an appropriate work-up and not treated with meclofenamate sodium.

**Hepatic Reactions**
As with other non-steroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in some patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (three times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with meclofenamate sodium. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with other non-steroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g.; eosinophilia, rash), meclofenamate sodium should be discontinued.

**Renal Effects**
As with other non-steroidal anti-inflammatory drugs, long-term administration of meclofenamate sodium to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome.
A second form of renal toxicity has been seen in patients with prerenal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly. Discontinuation of NSAID therapy is typically followed by recovery to the pretreatment state.
Since meclofenamate sodium metabolites are eliminated primarily by the kidneys, patients with significantly impaired renal function should be closely monitored; a lower daily dosage should be employed to avoid excessive drug accumulation.

**Information for Patients**
Patients should be advised that nausea, vomiting, diarrhea, and abdominal pain have been associated with the use of meclofenamate sodium. The patient should be made aware of a possible drug connection and accordingly should consider discontinuing the drug and contacting his or her physician if any of these conditions are severe.
Women who are taking meclofenamate sodium for heavy menstrual flow should be advised to consult their doctor if they have spotting or bleeding between cycles or worsening of their menstrual blood flow. These symptoms may be signs of the development of a more serious condition that is not appropriately treated with meclofenamate sodium.
Meclofenamate sodium may be taken with meals or milk to control gastrointestinal complaints. Concomitant administration of an antacid (specifically, aluminum and magnesium hydroxides) does not interfere with the absorption of the drug.
Meclofenamate sodium, like other drugs of its class, is not free of side effects. The side effects of these drugs can cause discomfort, and rarely, there are more serious side effects, such as gastrointestinal bleeding, which may result in hospitalization and even fatal outcomes.
NSAIDs (non-steroidal anti-inflammatory drugs) are often essential agents in the management of arthritis and have a major role in the treatment of pain, but they also may be commonly employed for conditions which are less serious.
Physicians may wish to discuss with their patients the potential risks (see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS) and likely benefits of NSAID treatment, particularly when the drugs are used for less serious conditions where treatment without NSAIDs may represent an acceptable alternative to both the patient and physician.

**Laboratory Tests**
Patients receiving long-term meclofenamate sodium therapy should have hemoglobin and hematocrit values determined if signs or symptoms of anemia occur.

Low white blood cell counts were rarely observed in clinical trials. These low counts were transient and usually returned to normal while the patient continued on meclofenamate sodium therapy. Persistent leukopenia, granulocytopenia, or thrombocytopenia warrant further clinical evaluation and may require discontinuation of the drug.
When abnormal blood chemistry values are obtained, follow-up studies are indicated.
Elevations of serum transaminase levels and of alkaline phosphatase levels occurred in approximately 4% of patients. An occasional patient had elevations of serum creatinine or BUN levels.
Because serious GI tract ulceration and bleeding can occur without warning symptoms, physicians should follow chronically treated patients for the signs and symptoms of ulceration and bleeding and should inform them of the importance of this follow-up (see WARNINGS: Risk of GI Ulceration, Bleeding and Perforation with NSAID Therapy).

**Drug Interactions**

1. Warfarin
Meclofenamate sodium enhances the effect of warfarin. Therefore, when meclofenamate sodium is given to a patient receiving warfarin, the dosage of warfarin should be reduced to prevent excessive prolongation of the prothrombin time.

2. Aspirin
Concurrent administration of aspirin may lower meclofenamate sodium plasma levels, possibly by competing for protein binding sites. The urinary excretion of meclofenamate sodium is unaffected by aspirin, indicating no change in meclofenamate sodium absorption. Meclofenamate sodium does not affect serum salicylate levels. Greater fecal blood loss results from concomitant administration of both drugs than from either drug alone.

3. Propoxyphene
The concurrent administration of propoxyphene hydrochloride does not affect the bioavailability of meclofenamate sodium.

4. Antacids
Concomitant administration of aluminum and magnesium hydroxides does not interfere with absorption of meclofenamate sodium.

**Carcinogenesis**
An 18 month study in rats revealed no evidence of carcinogenicity.

**Pregnancy**
Meclofenamate sodium, like aspirin and other non-steroidal anti-inflammatory drugs, causes fetotoxicity, minor skeletal malformations, e.g., supernumerary ribs, and delayed ossification in rodent reproduction trials, but no major teratogenicity. Similarly, it prolongs gestation and interferes with parturition and with normal development of young before weaning. Meclofenamate sodium is not recommended for use during pregnancy, particularly in the 1st and 3rd trimesters based on these animal findings. There are, however, no adequate and well controlled studies in pregnant women.

**Nursing Mothers**
Trace amounts of meclofenamic acid are excreted in human milk. Because of the possible adverse effects of prostaglandin-inhibiting drugs on neonates, meclofenamate sodium is not recommended for nursing women.

**Pediatric Use**
Safety and effectiveness in children below the age of 14 have not been established.

**ADVERSE REACTIONS**

**Incidence Greater Than 1%**
The following adverse reactions were observed in clinical trials and included observations from more than 2,700 patients, 594 of whom were treated for one year and 248 for at least two years.
***Gastrointestinal:*** The most frequently reported adverse reactions associated with meclofenamate sodium involve the gastrointestinal system. In controlled studies of up to six months duration, these disturbances occurred in the following decreasing order of frequency with the approximate incidences in parentheses: diarrhea (10% to 33%), nausea with or without vomiting (11%), other gastrointestinal disorders (10%), and abdominal pain[1]. In long-term uncontrolled studies of up to four years duration, one third of the patients had at least one episode of diarrhea some time during meclofenamate sodium therapy.
In approximately 4% of the patients in controlled studies, diarrhea was severe enough to require discontinuation of meclofenamate sodium. The occurrence of diarrhea is dose related, generally subsides with dose reduction, and clears with termination of therapy. The incidence of diarrhea in patients with osteoarthritis is generally lower than that reported in patients with rheumatoid arthritis.
Other reactions less frequently reported were pyrosis[1], flatulence[1], anorexia, constipation, stomatitis, and peptic ulcer. The majority of the patients with peptic ulcer had either a history of ulcer disease or were receiving concomitant anti-inflammatory drugs, including corticosteroids which are known to produce peptic ulceration.

***Cardiovascular:*** edema
***Dermatologic:*** rash[1], urticaria, pruritus
***Central Nervous System:*** headache[1], dizziness[1]
***Special Senses:*** tinnitus

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**1**Incidence between 3% and 9%. Those reactions occurring in 1% to 3% of patients are not marked with an asterisk.

**Incidence Less Than 1%—Probably Causally Related**
The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions.
***Gastrointestinal:*** bleeding and/or perforation with or without obvious ulcer formation, colitis, cholestatic jaundice
***Renal:*** renal failure
***Hematologic:*** neutropenia, thrombocytopenic purpura, leukopenia, agranulocytosis, hemolytic anemia, eosinophilia, decrease in hemoglobin and/or hematocrit
***Dermatologic:*** erythema multiforme, Stevens-Johnson Syndrome, exfoliative dermatitis
***Hepatic:*** alteration of liver function tests
***Allergic:*** lupus and serum sickness-like symptoms

**Incidence Less Than 1%—Causal Relationship Unknown**
Other reactions have been reported but under conditions where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to alert physicians.
***Cardiovascular:*** palpitations
***Central Nervous System:*** malaise, fatigue, paresthesia, insomnia, depression
***Special Senses:*** blurred vision, taste disturbances, decreased visual acuity, temporary loss of vision, reversible loss of color vision, retinal changes including macular fibrosis, macular and perimacular edema, conjunctivitis, iritis
***Renal:*** nocturia
***Gastrointestinal:*** paralytic ileus
***Dermatologic:*** erythema nodosum, hair loss

## OVERDOSAGE

The following is based on the little information available concerning overdosage with meclofenamate sodium and related compounds. After a massive overdose, CNS stimulation may be manifested by irrational behavior, marked agitation and generalized seizures. Following this phase, renal toxicity (falling urine output, rising creatinine, abnormal urinary cellular elements) may be noted with possible oliguria or anuria and azotemia. A 24 year-old male was anuric for approximately one week after ingesting an overdose of 6 to 7 grams of meclofenamate sodium. Spontaneous diuresis and recovery subsequently occurred.
Management consists of emptying the stomach by emesis or lavage and instilling an ample dose of activated charcoal into the stomach. There is some evidence that charcoal will actively absorb meclofenamate sodium, but dialysis or hemoperfusion may be less effective because of plasma protein binding. The seizures should be controlled by an appropriate anticonvulsant regimen. Attention should be directed throughout, by careful monitoring, to the preservation of vital functions and fluid-electrolyte balance. Dialysis may be required to correct serious azotemia or electrolyte imbalance.

## DOSAGE AND ADMINISTRATION

### Usual Dosage

For Mild to Moderate Pain
The recommended dose is 50 mg every 4 to 6 hours. Doses of 100 mg may be needed in some patients for optimal pain relief (see CLINICAL PHARMACOLOGY). However, the daily dose should not exceed 400 mg (see ADVERSE REACTIONS).

For excessive menstrual blood loss and primary dysmenorrheal
The recommended dose of meclofenamate sodium is 100 mg three times a day, for up to six days, starting at the onset of menstrual flow.

For rheumatoid arthritis and osteoarthritis (including acute exacerbations of chronic disease)
The dosage is 200 to 400 mg per day, administered in three or four equal doses.

Therapy should be initiated at the lower dosage, then increased as necessary to improve clinical response. The dosage should be individually adjusted for each patient, depending on the severity of the symptoms and the clinical response. The daily dosage should not exceed 400 mg per day. The smallest dosage of meclofenamate sodium that yields clinical control should be employed.

Although improvement may be seen in some patients in a few days, two to three weeks of treatment may be required to obtain the optimum therapeutic benefit.

After a satisfactory response has been achieved, the dosage should be adjusted as required. A lower dosage may suffice for long-term administration.

If gastrointestinal complaints occur (see WARNINGS and PRECAUTIONS), meclofenamate sodium may be administered with meals or with milk (see CLINICAL PHARMACOLOGY for a description of food effects). If intolerance occurs, the dosage may need to be reduced. Therapy should be terminated if any severe adverse reactions occur.

**HOW SUPPLIED**

Meclofenamate Sodium Capsules, USP are available containing either 50 mg or 100 mg of meclofenamic acid as the sodium salt.

The 50 mg capsule is a hard-shell gelatin capsule with a coral opaque cap and a coral opaque body axially printed with **MYLAN** over **2150** in black ink on both the cap and body. The capsule is filled with an off-white powder blend. They are available as follows:

NDC 0378-2150-01
bottles of 100 capsules

The 100 mg capsule is a hard-shell gelatin capsule with a coral opaque cap and a white opaque body axially printed with **MYLAN** over **3000** in black ink on both the cap and body. The capsule is filled with an off-white powder blend. They are available as follows:

NDC 0378-3000-01
bottles of 100 capsules
NDC 0378-3000-05
bottles of 500 capsules

**Store at 20° to 25°C (68° to 77°F). [See USP for Controlled Room Temperature.]**
**Protect from light and moisture.**
Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

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